REMARKS

After entry of this amendment, the claims pending are claims 1, 2, 4-10, 12-15 and 21-23. Claims 1 and 15 are amended and claims 21 to 23 are added to clarify the subject matter of the invention. Support for these amendments is found in the specification and particularly on pages 76-78, 80-81, and 88-89. No new matter is introduced by this amendment.

Any subject matter canceled from the claims by amendment is reserved for refiling in a continuation application filed during the pendency of this application. Applicants further affirm the correctness of the inventive entity in view of the cancellation of claims.

Rejections Under 35 USC §103(a)

> Claims 1, 2, 4-10 and 12-15 are rejected under 35 USC §103(a) as being unpatentable over US Patent No. 5,968,749 (Chang II) and US Patent No. 5,484,727 (Chang I) in view of US Patent No. 5,801,154 ("Baracchini").
>
> The examiner contends that Chang I and II recite oligonucleotide compounds for the inhibition of ACAT. Chang I and II are held to disclose the targeting of regions identical to that of Applicant's claim 1, the coding and start codon regions. Baracchini is held to teach use of antisense compounds 8-50 nucleotides in length to target and inhibit genes. Thus, combination of the cited references is held to teach all elements of the invention.

Applicants respectfully request reconsideration withdrawal of this rejection in view of the above amendments to the claims and the following remarks.

A. Chang I/II do not provide sufficient information to suggest the antisense compounds of the present claims.

Chang I and Chang II have the same specification and disclosure, and are hereinafter referred to collectively as Chang. Chang refers to the cloning of a nucleic acid molecule

encoding a human acyl coenzyme A:cholesterol actltransferase (ACAT), and the provision of a cell ***transformed with*** that nucleic acid molecule. The documents further teach a ***method of testing*** for an agent capable of inhibiting an ACAT by exposing an "agent" to a non-human cell transfected with a specific coding sequence for the ACAT and then inspecting the cell for inhibition of the ACAT enzyme activity. Among the ***non-specified*** agents which ***may be so tested*** are small organic molecules, antisense DNA or RNA (claim 2). The portion of the Chang specification that refers to the antisense compounds (see col. 5, lines 5-30 of Chang II) is extremely generic and can be found in any reference or review article discussing antisense technology. Chang states that the targeted sequence can be located in the coding region, or in a signal sequence (col. 5, lines 25-27).

Thus, in fact, Chang does no more than provide a ***method for testing*** for inhibitory activity of a generic antisense compound for which no description is provided. No specific antisense compositions are disclosed or suggested by these documents. None of this teaching leads one to the specific sequences of the ACAT of SEQ ID NO: 3 referred to by Applicants' amended claims. Chang does not refer to any minimal level of inhibition of ACAT expression that is desirable. Moveover, Chang does not disclose methods of using such antisense compounds to inhibit endogenous ACAT expression in cells or tissues, such as provided by Applicants' amended claim 15.

B. The Combination of Chang I/II with Baracchini Does Not Suggest the Presently Amended Claims.

Baracchini adds nothing to Chang that makes obvious the subject matter of the presently amended claims. In fact, taken for it generic antisense teachings, Baracchini does no more or less than simply reiterate Chang's generic teachings

about antisense sequence. In fact Baracchini refers to antisense compounds that modulute a completely unrelated protein to ACAT, namely multi-drug resistance-associated protein (MRP). Baracchini contains no disclosure that suggests or refers to the protein ACAT. Without any disclosure of ACAT, Baracchini cannot provide any suggestion that permits one to identify or suggest specific ACAT sequences of SEQ ID NO: 3 as target sequences for binding by a specific antisense sequence or provide any desired minimal level of inhibitory activity of ACAT antisense compounds. Baracchini does not teach or suggest any sequence for antisense compounds that bind to ACAT, as required by claim 1. Nor does Baracchini suggest any methods for using the sequences of claim 1. Baracchini does not teach or suggest a therapeutic utility of antisense compounds that bind ACAT.

Baracchini does not add anything to Chang that would make obvious the invention of the pending amended claims.

In fact, Applicants respectfully submit that an obviousness rejection based on a combination of Baracchini's generic disclosures about antisense sequences in general (and specifically with regard to MRP) and Chang's disclosure of a method of testing an inhibitory agent to ACAT, which agent may be ***an unidentified, unspecific*** antisense sequence, is defective. An obviousness rejection cannot be made by combining documents to make the bald suggestion that it is "obvious to try" to make antisense compounds to target ACAT.

Applicants are not claiming any and all antisense sequences that target any ACAT. Rather, Applicants' claims recite only sequences between 8 and 50 nucleobases in length that specifically hybridize within nucleotides 14-1741 of SEQ ID NO: 3 and which inhibit expression of the resulting enzyme by at least 12%.

The combination of Chang and Baracchini does not make the subject matter of these amended claims obvious. Taking each reference as a whole, the combination of

Baracchini and Chang does not provide any *suggestion* of Applicants' specificly-claimed antisense sequences, nor the method of claim 15.

In view of the above amendments and these remarks, Applicants' respectfully request that the examiner withdraw the outstanding rejections and permit the above pending claims to pass to issue in due course.

Supplement Information Disclosure Statement

The attached supplemental IDS cites to the examiner Applicants' co-pending US application relating to a different ACAT sequence. The ACAT sequence of the present claims and the ACAT sequence of the copending application claims have been compared and demonstrate no significant sequence homology. The IDS also recites documents cited in the international search report corresponding with this copending application and other documents. The documents are cited for completion of the IDS. None of these documents is believed to be more significant than the documents presently on record.

The Director is hereby authorized to charge any additional fees required with the filing of this paper or credit any overpayment in any fees to our deposit account number 08-3040.

Respectfully submitted,

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